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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Docket: LP-2005

Applicants : GRIFFITHS, Gareth-John, et al.  
Serial No. : 10/584,848  
Filed : June 28, 2006  
Title : METHOD FOR THE PRODUCTION OF 3-AMINO-5-(HYDROXYMETHYL)CYCLOPENTANE-1,2-DIOL-DERIVATIVES

TRANSMITTAL OF WRITTEN OPINION

Mail Stop Patent Application  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

Enclosed is a copy of the Written Opinion Of The International Searching

Authority from applicants' corresponding International patent application.

Respectfully submitted,

August 11, 2006  
Date

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**CERTIFICATE OF MAILING**

I hereby certify that this correspondence of is being deposited with the United States Postal Service as first class mail in an envelope addressed to: Mail Stop Patent Application, Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on

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# PATENT COOPERATION TREATY

From the  
INTERNATIONAL SEARCHING AUTHORITY

To:

see Form PCT/ISA/220

## PCT

WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY

(PCT Rule 43bis.1)

Date of mailing  
(day/month/year) see Form PCT/ISA/210 (sheet 2)

Applicant's or agent's file reference  
see Form PCT/ISA/220

### FOR FURTHER ACTION

See paragraph 2 below

International application No.  
PCT/EP2005/000643

International filing date (day/month/year)  
24.01.2005

Priority date (day/month/year)  
30.01.2004

International Patent Classification (IPC) or both national classification and IPC  
C07D317/44, C07D491/08, C07D209/52

Applicant  
LONZA AG

**1. This opinion contains indications relating to the following items:**

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☒ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43bis.1 (a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☒ Box No. VIII Certain observations on the international application

**2. FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA") except that this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notified the International Bureau under Rule 66.1bis(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of 3 months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires earlier.

For further options, see Form PCT/ISA/220.

**3. For further details, see notes to Form PCT/ISA/220.**

**Name and mailing address of the ISA**



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**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/EP2005/000643

**Box No. I. Basis of this opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.
  - ☐ This opinion has been established on the basis of a translation from the original language into the following language, which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).
2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:
  - a. type of material
    - ☐ a sequence listing
    - ☐ table(s) related to the sequence listing
  - b. format of material
    - ☐ in written format
    - ☐ in computer readable form
  - c. time of filing/furnishing
    - ☐ contained in the international application as filed.
    - ☐ filed together with the international application in computer readable form.
    - ☐ furnished subsequently to this Authority for the purposes of search.
3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.
4. Additional comments:

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/EP2005/000643

**Box No. IV Lack of unity of invention**

1. ☒ In response to the invitation (Form PCT/ISA/206) to pay additional fees the applicant has:
  - ☐ paid additional fees
  - ☐ paid additional fees under protest
  - ☒ not paid additional fees
2. ☐ This Authority found that the requirement of unity of invention is not complied with and chose not to invite the applicant to pay additional fees.
3. This Authority considers that the requirement of unity of invention in accordance with Rule 13.1, 13.2 and 13.3 is:
  - ☐ complied with
  - ☒ not complied with for the following reasons:  
**see separate sheet**
4. Consequently, this opinion has been established in respect of the following parts of the international application:
  - ☐ all parts
  - ☒ the parts relating to claims Nos. 1-14(partial), 15-17(complete)

**Box No. V Reasoned statement under Rule 43b/s.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

|                               |                  |
|-------------------------------|------------------|
| Novelty (N)                   | Yes: Claims 1-17 |
|                               | No: Claims       |
| Inventive Step (IS)           | Yes: Claims      |
|                               | No: Claims 1-17  |
| Industrial Applicability (IA) | Yes: Claims 1-17 |
|                               | No: Claims       |

2. Citations and explanations:

**see separate sheet**

**WRITTEN OPINION OF THE  
INTERNATIONAL SEARCHING AUTHORITY**

International application No.  
PCT/EP2005/000643

**Box No. VIII: Certain observations on the international application**

The following observations on the clarity of the claims, descriptions, and drawings or on the question whether the claims are fully supported by the description, are made:

**see separate sheet**

**Point IV**

**Lack of unity of invention**

The present application is concerned with a method for preparing 4-substituted 2,3-isopropylidenedioxocyclopentan-1-amines of the formula I and salts of these compounds with dibasic or tribasic organic acids. Present claims 1-14 are directed both at the free amines and at the salts.

Two groups of inventions emerge:

1. Claims 1-14 (in part), 15-17 (wholly):

Methods (steps a) to e)) and intermediates for preparing free 4-substituted 2,3-isopropylidenedioxocyclopentan-1-amines of the formula I

2. Claims 1-14 (in part), 18 (wholly)

Salts of 4-substituted 2,3-isopropylidenedioxocyclopentan-1-amines of the formula I with dibasic or tribasic organic acids and method (step f)) for preparing them.

A European patent application may comprise only a single invention or a group of inventions which are linked by a common inventive concept (PCT Rule 13.1). Unity is present only if there is a technical relationship between the inventions involving one or more special technical features. By "special technical features" are meant those technical features that define a contribution which the claimed invention makes over the prior art (PCT Rule 13.2).

The subject matter of the two groups of inventions includes the free 4-substituted 2,3-isopropylidenedioxocyclopentan-1-amines as the sole common feature. However, said compounds belong to the prior art (e.g. D1, D2) and therefore do not represent a "special technical feature". Correspondingly, the two groups mentioned are directed at two different problems and thus at two different inventions:

Group 1: alternative process for preparing free 4-substituted 2,3-isopropylidenedioxocyclopentan-1-amines starting from known azabicycles

Group 2: preparation of further salts of dibasic or tribasic organic acids starting from known free 4-substituted 2,3-isopropylidenedioxocyclopentan-1-amines.

Further examination below is based on the invention for which a search report is available, that is invention (1).

**Point V**

**Reasoned statement with regard to novelty, inventive step and industrial applicability; citations and explanations supporting such statement**

1 Reference is made to the following documents. The same numbering for the documents will be used throughout the procedure:

D1: O 02/091988 A (AVENTIS PHARMA INC) 21 November 2002

D2: WO 00/23447 A (MYERS MICHAEL R; CHOI SLEDESKI YONG MI (US); PAULS HEINZ W (US); EWIN) 27 April 2000

D3: WO 97/03053 A (RHONE-POULENC RORER PHARMA; PETRE DOMINIQUE (FR); DARNAND ELIANE (FR)) 30 January 1997

D4: US-A-5 684 159 (LARGEAU DENIS ET AL) 4 November 1997

D5: WO 00/03032 A (BRUX FRANK; GUGGISBERG YVES (CH); LONZA AG (CH); WERBITZKY OLEG (CH)); 20 January 2000

2 D1 and D2 are the most relevant prior art documents and disclose synthetic routes comparable to the present route II → III → IV → V → I. The present method represents a novel selection from the closest method of D1, since the general protective group P is mentioned but acetyl is not specifically mentioned as protective group. BOC is mentioned as exemplary protective group. The subject matter of invention 1 is accordingly novel (PCT Article 33(2)).

3 The present technical problem consists of providing an alternative method for preparing known, free 4-substituted 2,3-isopropylidenedioxocyclopentan-1-amine starting from known aza bicycles. The solution involves the use of a particular protective group (Ac) in a multistage method which is otherwise the same. The selection of a particular protective group without an advantageous surprising effect achieved thereby compared with the closest prior art (D1, Example 3) is not to be regarded as an inventive selection. Accordingly, the claims of invention 1 are at present not to be regarded as inventive (PCT Article 33(3)).

4 The present claims are industrially applicable and meet the requirements of PCT Article 33(4).

Point VIII

**Certain observations on the international application**

The method detailed by way of example in the present application for preparing compounds of the formula I with  $R^2 = R^3 = \text{Me}$  is not encompassed by the claims. Accordingly, the present claims are not based on the description within the meaning of PCT Article 6 and disclosed in the patent application within the meaning of PCT Article 5.